

CLAIMS

What is claimed is:

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1. A method of increasing in a mammal a population of hematopoietic stem cells which are capable of undergoing normal hematopoiesis, differentiation and maturation in hematopoietic tissue, comprising contacting the hematopoietic tissue with at least one inhibitor of nitric oxide synthase, thereby producing hematopoietic tissue having an increased population of hematopoietic stem cells which are capable of undergoing normal hematopoiesis, differentiation and maturation.
 - 10 2. The method of Claim 1 wherein the inhibitor is contacted with the hematopoietic tissue for a period of days selected from the group consisting of: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 days.
 3. A method according to Claim 1 wherein the step of contacting is carried out *ex vivo*.
 - 15 4. A method according to Claim 3 further comprising transplanting the hematopoietic tissue having an increased population of hematopoietic stem cells into a mammal in need thereof.
 5. A method according to Claim 1 wherein the differentiation of erythroid cells is prevented.
 - 20 6. A method according to Claim 1 wherein the differentiation of myeloid cells is prevented.

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7. A method according to Claim 1 further comprising contacting the hematopoietic tissue with at least one hematopoietic growth factor selected to induce differentiation of a selected hematopoietic stem cell population.
- 5 8. A method according to Claim 1 wherein the inhibitor of nitric oxide synthase is selected from the group consisting of L-nitroarginine methyl ester, 2-ethyl-2-thiopseudourea, aminoguanidine hemisulfate and N-monomethyl-L-arginine.
- 10 9. A method for treating a mammal to increase a population of hematopoietic stem cells which are capable of undergoing normal hematopoiesis, differentiation and maturation in hematopoietic tissue of the mammal, comprising contacting the hematopoietic tissue of the mammal with at least one inhibitor of nitric oxide synthase, thereby producing hematopoietic tissue having an increased population of hematopoietic stem cells which are capable of undergoing normal hematopoiesis, differentiation and maturation.
- 15 10. The method of Claim 9 wherein the inhibitor is contacted with the hematopoietic tissue for a period of days selected from the group consisting of: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 days.
11. A method according to Claim 9 further comprising contacting the hematopoietic tissue with at least one hematopoietic growth factor selected to induce differentiation of a selected hematopoietic stem cell population.
- 20 12. A method for treating a mammal to increase a population of hematopoietic stem cells which are capable of undergoing normal hematopoiesis, differentiation and maturation in hematopoietic tissue of the mammal, comprising the steps of:
- a) obtaining hematopoietic tissue which is to be transplanted into the mammal;

- b) contacting the hematopoietic tissue to be transplanted
with at least one inhibitor of nitric oxide synthase;
c) transplanting the hematopoietic tissue of step (b) into the mammal to be
treated,

5 thereby providing the mammal with hematopoietic tissue having an increased
population of hematopoietic stem cells which are capable of undergoing normal
hematopoiesis, differentiation and maturation.

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13. The method of Claim 12 wherein the inhibitor is contacted with the
hematopoietic tissue for a period of days selected from the group consisting of: 1,
10 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 days.

14. A method according to Claim 12 further comprising:
d) treating the mammal with an enhancer of nitric
oxide synthase after transplanting the hematopoietic tissue.

15. A method according to Claim 12 further comprising:
15 d) treating the mammal with an inhibitor of nitric
oxide synthase after transplanting the hematopoietic tissue.

16. A method of increasing a population of progenitor blood cells which are capable
of undergoing normal hematopoiesis, differentiation and maturation, comprising
contacting progenitor cells of blood with at least one inhibitor of nitric oxide
20 synthase, thereby increasing the population of progenitor blood cells.

17. The method of Claim 16 wherein the inhibitor is contacted with the blood for a
period of days selected from the group consisting of: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10,
11 and 12 days.

18. A method according to Claim 16 wherein the progenitor cells of the blood are obtained from hematopoietic tissue selected from the group consisting of: bone marrow, umbilical cord vein blood, peripheral blood, fetal liver and long term hematopoietic cell cultures.
- 5 19. A method according to Claim 16 wherein the inhibitor of nitric oxide synthase is selected from the group consisting of L-nitroarginine methyl ester, 2-ethyl-2-thiopseudourea, aminoguanidine hemisulfate and N-monomethyl-L-arginine.
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20. A method of increasing a population of dividing cells in a tissue of a mammal comprising contacting the cells with at least one inhibitor of nitric oxide.
- 10 21. A method according to Claim 20 wherein the inhibitor is an inhibitor of nitric oxide synthase.
22. A method according to Claim 20 which results in an increase in the size of an organ with which the tissue is associated.
- 15 23. A method of decreasing a population of cells in S phase in a tissue of a mammal and inducing differentiation of the cells, comprising contacting the tissue with at least one enhancer of nitric oxide.
24. A method according to Claim 23 wherein the enhancer is an enhancer of nitric oxide synthase.
- 20 25. A method according to Claim 23 which results in a decrease in the size of an organ with which the tissue is associated.

26. A method of coordinating developmental decisions of a cell type in a mammal, comprising introducing nitric oxide into the cell type or precursor of the cell type, thereby inhibiting proliferation of the cell type or precursor of the cell type and inducing differentiation of the cell type or precursor of the cell type.
- 5 27. A method of inducing differentiation in a mammalian cell population comprising contacting the cell population with nitric oxide or a nitric oxide enhancer.
28. A method of regenerating tissue in an adult mammal comprising contacting a selected tissue with at least one inhibitor of nitric oxide, thereby inhibiting differentiation and inducing proliferation of cells of the tissue, then contacting
10 the selected tissue with a compound which inhibits proliferation and induces differentiation.
29. The method of Claim 28 wherein the compound which inhibits proliferation and induces differentiation is selected from the group consisting of: nitric oxide, a growth factor, or a combination of both.
- 15 30. The method of Claim 28 wherein the inhibitor of nitric oxide is an inhibitor of nitric oxide synthase.
31. The method of Claim 28 which results in an increase in the size of an organ with which the tissue is associated.
- 20 32. A method according to Claim 28, wherein the tissue is selected from the group consisting of blood, skin, bone, digestive epithelium, fat tissue, bone marrow stroma, cartilage and tendon.

33. A method of repopulating an organ or tissue having normally nondividing cells comprising contacting a selected organ or tissue with at least one inhibitor of nitric oxide, thereby inhibiting differentiation and inducing proliferation of cells of the organ or tissue, then contacting the selected organ or tissue with a compound which inhibits proliferation and induces differentiation.
34. The method of Claim 33 wherein the compound which inhibits proliferation and induces differentiation is selected from the group consisting of: nitric oxide, a growth factor, or a combination of both.
35. The method of Claim 33 wherein the inhibitor of nitric oxide is an inhibitor of nitric oxide synthase.
36. The method of Claim 33 which results in an increase in the size of the organ.
37. A method according to Claim 33 wherein the organ or tissue is selected from the group consisting of muscle and nerve fibers.
38. A method of producing a subpopulation of hematopoietic cells in hematopoietic tissue comprising the steps of:
- contacting the hematopoietic tissue with at least one inhibitor of nitric oxide synthase, thereby producing hematopoietic tissue having an increased population of hematopoietic stem cells which are capable of undergoing normal hematopoiesis, differentiation and maturation; and
 - contacting the hematopoietic tissue with at least one hematopoietic growth factor selected to induce specific differentiation of the hematopoietic stem cell population, thereby producing a subpopulation of hematopoietic tissue.

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39. The method of Claim 38 wherein the inhibitor is contacted with the bone marrow for a period of days selected from the group consisting of: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 days.

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5 40. A method according to Claim 38 wherein the inhibitor of nitric oxide synthase is selected from the group consisting of L-nitroarginine methyl ester, 2-ethyl-2-thiopseudourea, aminoguanidine hemisulfate and N-monomethyl-L-arginine.

11/4/03 41. A method of increasing a ^{population of} ~~population~~ of cells in S phase in a tissue of a mammal, comprising contacting the tissue ^{with an} ~~with an~~ inhibitor of nitric oxide.

11/4/03 42. A method according to Claim 41 wherein ^{the} ~~the~~ cells in S phase can be used in gene therapy.
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